

REMARKS

Status of the claims:

With the above amendments, claims 15 and 16 have been cancelled, claims 1, 6, 13, and 14 have been amended, and claims 17-39 have been added. Thus, claims 1-14 and 17-39 are pending and ready for further action on the merits. No new matter has been incorporated by way of the above amendments. Reconsideration in light of the following remarks is respectfully requested.

Claim Objections

Claims 7 and 13 are objected to for having spelling informalities. The Examiner asserts that claim 7 has "adstringent" misspelled and claim 13 has "topic" misspelled.

Regarding claim 7, Applicants assert that the spelling "adstringent" is correct. As proof of this, Applicants submit page 16 from Grant and Hackh's Chemical Dictionary, Fifth Edition, ed. Grant, R. and Grant, C., McGraw-Hill, New York, 1987.

Claim 13 has been amended so that it no longer contains the word "topic". It is believed that with these changes and explanations that the objection has been obviated. Withdrawal of the rejections is respectfully requested.

Rejections under 35 USC §112, second paragraph

Claims 1, 5, 6, and 13-16 have been rejected under 35 USC §112, second paragraph as being indefinite. The Examiner asserts that "at least one trace element" is unclear because claims 1-3 require a metal salt or minerals. This rejection is traversed for the following reasons.

Applicants assert that the term "at least one trace element" is neither unclear nor indefinite. The terms "alkali metal salts" and "alkaline earth metal salts" are generally used terms which are within the common knowledge of a person skilled in the art. Therefore, a person skilled in the art knows very well usual examples of alkali metal salts as well as usual examples of alkaline earth metal salts.

Further, examples of these salts can be found in textbooks frequently used in the art. Moreover, examples, particularly of trace elements, are disclosed in the present application on page 6, lines 7 to 12. Accordingly, Applicants submit that the phrase, "at least one trace element" is neither vague nor indefinite. Withdrawal of the rejection is warranted and respectfully requested.

The Examiner asserts that "at least one liposome" in claim 6 is indefinite because it is unclear how a topical composition can contain only one liposome. Applicants traverse.

Applicants submit that there is nothing vague or indefinite about this phrase. A liposome is a lipid bilayer that forms a spherical conglomerate. Thus, "at least one liposome" is one or more liposome particles that can be of diverse composition.

It is believed that with this explanation that any ambiguity has been removed. Withdrawal of the rejection is respectfully requested.

Claims 1 and 13-16 are rejected under 35 USC §§101 and 112, second paragraph for reciting "use" claims. Claims 1 and 13-14 have been converted to "method of use" claims and claims 15 and 16 have been canceled. It is believed that with these changes and cancellations, that the rejection has been obviated. Withdrawal of the rejection is respectfully requested.

Rejections under 35 USC §102

Claim 1 has been rejected under 35 USC §102(b) as being anticipated by Abad '740 (US Patent No. 5,538,740). This rejection is traversed for the following reasons.

The Examiner asserts that Abad '740 discloses a therapeutic and cosmetic composition containing calcium carbonate, zinc oxide, polyethylene glycol, and amino acids. Although Applicants do not dispute that these elements are disclosed in Abad '740, Applicants were unable to find one example that had all of these elements. Thus, Applicants assert that an anticipatory rejection is

inappropriate.

Abad '740 describes a method for preparing an active ingredient for use in therapeutic or cosmetic compositions, which comprises centrifuging a live *Helix* gastropod for a time and at a gravity sufficient to cause the gastropod to secrete a fluid containing the active ingredient but not to kill the gastropod, and recovering the secretion containing the active ingredient which consists essentially of a mixture of amino acids and non-toxic substances secreted from the gastropod. The Abad '740 composition comprising the gastropod secretion and an excipient can be applied to the skin and is used for preventing and treating certain medical indications as disclosed in column 3, lines 30 to 44. The excipient comprises a multiplicity of substances as disclosed in the paragraph bridging columns 6 and 7, examples of which are calcium carbonate and zinc oxide. Example III of Abad '740 (see column 9, lines 22 *et seq.*) indicates that the secretions comprise amino acids as well as atoxic substances without therapeutic value. Example 'V' e.g. uses a liquid secretion and the excipient of example IV.

The present invention is novel over Abad '740 because the present invention discloses and claims amino acids that are **added in pure form** and not in the form of secretions comprising an arbitrary mixture of amino acids in combination with further

substances, the effects of which are not clearly disclosed in Abad '740.

Contrary to the secretions used in Abad '740, which comprise an arbitrary mixture of certain amino acids and further undefined substances, the present invention discloses and claims the amino acids in pure form. This has the advantage that specific amino acids can be specifically added to the inventive preparation in order to induce the desired effects or to administer those specific amino acids, which are particularly used for treating a specific medical condition.

For the reasons above, Applicants submit that the anticipatory rejection over Abad '740 is inapposite. Withdrawal of the rejection is warranted and respectfully requested.

Rejections under 35 USC §103

Claims 2, 5-7, 9-11, 14, and 16 have been rejected under 35 USC §103(a) as being unpatentable over Abad '740 (US Patent No. 5,538,740) in combination with Pickart '375 (US Patent No. 5,554,375).

Claims 3, 4, 13, and 15 have been rejected under 35 USC §103(a) as being unpatentable over Abad '740 in combination with Pickart '375 and further in view of Horrobin '686 (US Patent No. 5,145,686).

These rejections are traversed for the following reasons.

Present Invention

The present invention relates to a method of treating medical conditions as specified in claim 1 comprising administering to a patient in need of such treatment a pharmaceutically effective amount of a preparation comprising (a) at least one salt selected from alkali metal salts, alkaline earth metal salts and other minerals (b) at least one pure amino acid and (c) zinc oxide and/or an inorganic peroxide.

Page 5, at the second to fourth paragraph indicates that the preparation of the present invention takes into account new research results concerning the diffusion of ions through ion channels into the intracellular space. The inventive preparation uses the principle of ion exchange between the cell interior and the cell exterior using high osmotic pressure, which is created by a combination of active substances of the preparation. In this process the amino acids help the ions to more effectively overcome the natural barriers of the cell membranes to reach the cell interior. Furthermore, in contrast to the salts alone, a combination of salts and amino acids has a greater positive effect on the skin physiology. When salts are used in combination with amino acids, the salts are infiltrated into the cell more effectively than without amino acids, as amino acids are on the one hand a key of the cell membranes and on the other, support and increase the activation of the ion channels. Therefore, the

present invention realizes the unexpected synergistic effect of salts and amino acids.

In combination with zinc oxide and/or inorganic peroxides a better infiltration of agents into and a better distribution of agents in the cell is obtained. That is, the inventive composition provides an improvement of microcirculation in the cells wherein the microcirculation is greater, more steady, lasts longer and approaches the starting value slowly compared, e.g. to the use of only salts.

The amino acids and amino acid derivatives can be used in the present invention solely or in the form of mixtures. The amino acids and their derivatives are preferably added in a pure form (see page 7, second paragraph). Zinc oxide and/or an inorganic peroxide can be used to regulate the osmotic pressure. Surprisingly, the combination of amino acids with zinc oxide and/or an inorganic oxide has a particularly good effect (see page 7, last paragraph).

Disclosure of Abad '740

As described above, Abad '740 describes a method for preparing an active ingredient for use in therapeutic or cosmetic compositions, which comprises centrifuging a live Helix gastropod for a time and at a gravity sufficient to cause the gastropod to secrete a fluid containing the active ingredient

but not to kill the gastropod, and recovering the secretion containing the active ingredient which consists essentially of a mixture of amino acids and non-toxic substances secreted from the gastropod. The Abad '740 composition comprising the gastropod secretion and an excipient can be applied to the skin and is used for preventing and treating certain medical conditions as disclosed in column 3, lines 30 to 44. The excipient comprises a multiplicity of substances as disclosed in the paragraph bridging columns 6 and 7, examples of which are calcium carbonate and zinc oxide. Example M of Abad '740 indicates that the secretions comprise amino acids as well as atoxic substances without therapeutic value. Example 'V' e.g. uses a liquid secretion and the excipient of example IV.

Disclosure of Pickart '375

Pickart '375 describes a composition for accelerating the healing of topical wounds and skin irritations prepared from peptones complexed with an ionic transition salt. A peptone digest is combined with an amount of an aqueous solution of transition metal salt sufficient to induce a precipitate. The resulting precipitate is composed of complexes of the hydrophobic peptides from the peptone and the metal (see column 4, lines 28 to 50). The peptone-metal complexes of Pickart '375 are prepared from enzymatic digests of proteins. Peptones are

generally comprised of intermediate polypeptide products and mixtures of small peptides, formed in partial hydrolysis of proteins. By peptone digest, it is meant that the protein is degraded by enzymatic digestion (see column 5, lines 28 to 36).

Removal of Abad '740 in combination with Pickart '375

The present invention cannot be rendered obvious by Abad '740 in combination with Pickart '375 because the amino acids of the present invention are added in pure form and not in form of secretions comprising an arbitrary mixture of amino acids in combination with further substances as disclosed in Abad '740. Pickart '375 does not make up this deficiency.

Accordingly, Applicants assert that the Examiner has failed to make out a *prima facie* case of obviousness with regard to the 35 USC §103(a) rejection over Abad '740 in combination with Pickart '375. Three criteria must be met to make out a *prima facie* case of obviousness.

- 1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.
- 2) There must be a reasonable expectation of success.
- 3) The prior art reference (or references when combined) must teach or suggest all the claim limitations.

See MPEP §2142 and *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). In particular, the Examiner has failed to meet the third element to make a *prima facie* obviousness rejection. Neither of the references disclose adding the amino acids in pure form. For this reason alone, the rejection is inapposite. Withdrawal of the rejection is warranted and respectfully requested.

Further, there is no suggestion or hint in Abad '740 pointing to unexpected synergistic effects of amino acids and salts as disclosed on page 5 of the present application. The calcium salt and zinc oxide comprised in the excipient of Abad '740 are only arbitrarily present. Also, Abad '740 does not provide any teaching or suggestion pointing to the synergistic effects as described in the present application, which improves microcirculation. Further, Abad '740 is silent concerning secondary plant substances and polyunsaturated fatty acids as required by present claims 2 and 3 of the present invention. Accordingly, the present invention would not be obvious to a person skilled in the art from the teaching of Abad '740.

The deficiencies of Abad '740 are not corrected by Pickart '375 because Pickart '375 does not describe or suggest a composition comprising at least one salt, at least one pure amino acid and zinc oxide and/or inorganic peroxide. Furthermore, there is also no teaching or suggestion in Pickart '375 pointing to the subject-matter of the present invention.

Moreover, Pickart '375 describes peptone-metal complexes prepared from enzymatic digests of proteins combined with transition metal salts. That is, the teaching of Pickart '375 relates to complexes of hydrophobic peptides from the peptone and the metal. There is no teaching or suggestion in Pickart '375 pointing to zinc oxide and/or inorganic peroxides.

Additionally, because Abad '740 describes secretions comprising amino acids and Pickart '375, contrary thereto, peptone-metal complexes, the combination of the references fails to describe use of pure amino acids.

Pickart '375 does disclose one example containing "aloe vera" where the aloe vera appears to be present by accident. However, there is no general suggestion in Pickart '375 pointing to any bio-active plant substances and their advantages and effects. Further, Pickart '375 discloses the above-described complexes but does not give any hint to the artisan of ordinary skill regarding the advantages/effects of bio-active plant substances. Because the teaching of Pickart '375 is based on peptone-metal complexes and not on "aloe vera", the subject-matter of the present invention would not be obvious to a person skilled in the art either by a combination of Abad '740 and Pickart '375, even if the skilled person would combine these references at all as indicated above. Therefore, Applicants

submit the rejection is made with knowledge of the present application, or in other words, by hindsight reconstruction.

Disclosure of Horrobin '686

Horrobin '686 describes a composition for topical administration comprising lithium salt and evening primrose oil. Horrobin '686 does not describe the use of zinc oxide and/or inorganic peroxides or the use of amino acids.

Removal of Abad '740 in combination with Pickart '375 and further in view of Horrobin '686

Because Horrobin '686 neither teaches nor suggests the subject matter of the present invention, the present invention is patentable over Abad '740 in combination with Pickart '375 and further in view of Horrobin '686.

There is no disclosure or suggestion in Horrobin '686 pointing to compositions comprising amino acids and zinc oxide and/or inorganic peroxides.

Moreover, because Horrobin '686 fails to disclose pure amino acids as does Abad '740 and Pickart '375, Applicants assert that the Examiner has failed to make out a *prima facie* case of obviousness with regard to the 35 USC §103(a) rejection over Abad '740 in combination with Pickart '375 and further in

view of Horrobin '686. As was pointed out above, three criteria must be met to make out a *prima facie* case of obviousness.

- 1) There must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings.
- 2) There must be a reasonable expectation of success.
- 3) The prior art reference (or references when combined) must teach or suggest all the claim limitations.

See MPEP §2142 and *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991). As was pointed out above, the Examiner has failed to meet the third element to make a *prima facie* obviousness rejection. Horrobin '686 does not make up the deficiencies of Abad '740 and Pickart '375 in their failure to disclose pure amino acids. Accordingly, no *prima facie* case of obviousness has been made. For this reason alone, withdrawal of the rejection is warranted and respectfully requested.

Furthermore, there is also no suggestion that would motivate a person skilled in the art to combine this reference with Abad '740 or Pickart '375. Please see *in re Dembiczak*, 50 USPQ2d 1614 (Fed Cir. 1999) regarding combining references. Therefore, the present invention cannot be rendered obvious over a combination of these references. Withdrawal of the rejection is warranted and respectfully requested.

With the above remarks and amendments, it is believed that the claims, as they now stand, define patentable subject matter such that a passage of the instant invention to allowance is warranted. A Notice to that effect is earnestly solicited.

If any questions remain regarding the above matters, please contact Applicant's representative, Andrew D. Meikle, in the Washington metropolitan area at the phone number listed below.


Pursuant to 37 C.F.R. §§ 1.17 and 1.136(a), Applicant(s) respectfully petition(s) for a three (3) month extension of time for filing a reply in connection with the present application, and the required fee of \$460.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachment: Grant & Hackh's Chemical Dictionary

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

Claims 15 and 16 have been deleted.

The claims have been amended as follows:

1. (Amended) [Use] A method of treating skin irritations, sun burn, cellulitis, wrinkles, acne, herpes, neurodermatitis, ozone damage, burns, caustic burns, thickenings, edemas, hematomas, hemorrhoids, rheumatism, arthrosis, or skin cancer comprising administering to a patient in need of such treatment a pharmaceutically effective amount of a preparation comprising:

(a) at least one salt selected from alkali metal salts, alkaline earth metal salts and other minerals,

(b) at least one amino acid added in a pure form, and

(c) zinc oxide and/or an inorganic peroxide

[for the preparation of a pharmaceutical composition for the treatment of skin irritations, sun burn, cellulitis, wrinkles, acne, herpes, neurodermatitis, ozone damage, burns, caustic burns, thickenings, edemas, hematomas, hemorrhoids, rheumatism, arthrosis, and skin cancer].

13. (Amended) [Use of a preparation according to claim 3 for topical administration] The method according to claim 3 where the preparation is administered topically.

14. (Amended) [Use of a preparation according to claim 2]
The method according to claim 2 where the preparation is
administered as a cosmetic.

Claims 17-39 have been added.

GRANT & HACKH'S CHEMICAL DICTIONARY

[*American, International, European and British Usage*]

*Containing the Words Generally Used in Chemistry,
and Many of the Terms Used in the Related
Sciences of Physics, Medicine, Engineering,
Biology, Pharmacy, Astrophysics,
Agriculture, Mineralogy, etc.*

Based on Recent Scientific Literature

FIFTH EDITION

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The previous edition of this book was *Hackh's Chemical Dictionary*,
4th ed., published by McGraw-Hill in 1969. It was prepared by Dr.
Julius Grant from a *Chemical Dictionary* compiled by Ingo W. D.
Hackh. The current, or 5th, edition of this book was prepared by Dr.
Roger L. Grant, whose father prepared the 4th edition.

*The editors for this book were Betty J. Sun and Susan Thomas,
the designer was Naomi Auerbach, and the production
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leaves and stems of *A. vernalis* (Ranunculaceae). The fluid extract is a heart stimulant.

adonite $C_5H_{12}O_5 = 152.1$. Adonitol. A pentahydric alcohol, from *Adonis vernalis*. Colorless prisms, m. 102, soluble in water.

adonitol Adonite.

ADP* Symbol for adenosine 5'-diphosphate.

adrenal gland An endocrine gland above each kidney, consisting of 2 histologically and functionally separate parts: the cortex, which secretes corticoid hormones and small quantities of sex hormones, and the medulla, which secretes epinephrine and norepinephrine.

Adrenalin Trademark for adrenaline, epinephrine.

adrenaline BP name for epinephrine.

Adrenine Trade name for epinephrine.

adrenolutine A fluorescent oxidation product of epinephrine.

Adriamycin Trademark for doxorubicin. a. hydrochloride Doxorubicin.

adsorbate That which is adsorbed.

adsorbent A substance that adsorbs, as, charcoal. Cf.

absorbent. *crystallogenic* ~ A crystalline substance which, when dehydrated without losing its shape, becomes porous and, thus, absorbent, e.g., chabazite.

adsorption The ability of a substance (*adsorbent*) to hold or concentrate gases, liquids, or dissolved substances (*adsorbate*) upon its surface; cf. *adhesion*, *sorption*, *absorption*, *desorption*, *persorption*, *wetting*. *anomal* ~ A. which does not follow the a. isotherm, as with certain colloidal dyes. *apolar* ~ Nonpolar a. *co* ~ A. in which two substances are held on a surface, which adsorbs neither alone. *differential* ~ See *differential adsorption*. *heat of* ~ The joules (or cal) liberated during a. *negative* ~ A. in which the surface concentration of the adsorbate is lowered by preferential a. of the liquid. *nonpolar* ~ Apolar. A. in which nonelectrolytes or equivalent ions of electrolytes are held on a surface. *oriented* ~ A. in which the molecules are grouped on the surface in a definite direction. *polar* ~ A. in which definite anions or cations are held in nonequivalent amounts. *positive* ~ A. in which the surface concentration of the adsorbate is relatively high. *preferential* ~ Pronounced a. of one substance compared with another of similar physical properties. *specific* ~ (1) Preferential a. (2) The quantity of adsorbate on 1 cm² of surface.

a. analysis Separation of mixtures by the different adsorbability of the components. Cf. *chromatographic analysis*.

a. catalysis A chemical reaction in which the adsorbent acts as a catalyst. a. coefficient The quantity x of the a. isotherm.

a. colorimetry The a. of colored substances from solution on a white adsorbent, and comparison of the separated and dried colored powders with standards, similarly prepared, in visible or ultraviolet light (a. fluorimetry). a. displacement The replacement of one adsorbate on a surface by another. a. equilibrium The distribution of molecules on a surface and in the surrounding medium. Cf. a. isotherm. a. exponent The quantity $1/n$ of the a. isotherm. a. fluorimetry See a. colorimetry. a. isotherm The approximate empirical relationship existing between the concentration x , held upon the surface, and the amount c , which is not adsorbed: $x/m = \alpha \cdot c^{1/n}$, where m is the amount of adsorbent, and α and $1/n$ are experimental constants. a. potential The work obtainable when an adsorbate is brought into the a. space.

adsorptive Adsorbate.

adstringent Astringent.

adubiri A fish poison from *Paulownia speciosa*, used in Ghana.

adularia A variety of orthoclase.

adularin A potassium silicate of uncertain composition.

adulterant A substance of cheaper or inferior quality, sometimes harmful, added to an article, compound, or food.

adulteration (1) The fraudulent addition of a foreign substance, especially harmful preservatives, to food products. (2) The removal of an essential constituent of a substance, as cream from milk.

advection Heating or cooling effects due to horizontal currents in air or water. Cf. *convection*.

adventitious Not typical or normal; accidental.

æ- See (1) *ae-*; (2) also *e-*.

aegerite Wurtzite.

aegirite Acmite.

aenigmatite Black, triclinic, amphibole metasilicate of sodium and ferrous iron, containing some titanium instead of silicon, d. 3.8.

aeolotropic Anisotropic.

aeonite Wurtzite.

aerated water A water artificially impregnated with oxygen or carbon dioxide, as, soda water.

aerator A machine to oxygenate effluent and thus reduce its B.O.D.

aerobe An organism that requires an atmosphere of oxygen for respiration. Cf. *anaerobe*.

aerobic bacteria Certain bacteria which require gaseous oxygen for growth. Cf. *anaerobic*.

aerobioscope A device to determine the number of bacteria in air.

aerobiosis Life sustained in an atmosphere containing oxygen.

aerodynamics Pneumatics. The study of the motion of gases.

Aerofloat Trademark for flotation agents of the dithiophosphoric acid type.

aeroklinoscope An air cell used to float algae on water.

aerolite A meteoric stone of silicates. Cf. *siderolite*.

aerometal An alloy: Al, with Cu 0.2-4, Fe 0.3-1.3, Mn 0-1.2, Mg 0-3, Zn 0-3, Si 0.5-1.0%. Cf. *acieral*.

aerometer An instrument to determine the density of gases.

aeron An aluminum alloy with Cu 1.5-2.0, Si 1.0, Mn 0.75%.

aeronomy The study of the upper atmosphere and especially its radiation and electromagnetic properties.

aerophone An apparatus to amplify sound waves.

aeroplankton Organisms (pollen, bacteria, etc.) carried by air.

aeroscope A glass apparatus to obtain bacteria from air.

aerosiderite An iron meteorite. Cf. *siderite*.

aerosite Pyrargyrite.

Aerosol (1) Trade name for a wetting agent of the sulfonated dicarboxylic acid ester type; e.g., A.-OT is sodium bis(2-ethylhexyl) succinic sulfonate. (2) (not cap.) A *colloidal system*, q.v., with gas as the surrounding medium; as, smokes and fogs. a. pressure packaging A method of dispensing cosmetics, medicaments, and similar products in the form of a gas-liquid aerosol spray. A homogeneous mixture of the product and a liquified gas (e.g., dichlorofluoroethane) in the pack under pressure is released by opening a valve.

aerosphere Atmosphere.

aerostatics The study of gases in mechanical equilibrium. Cf. *hydrostatics*.

aerotherapeutics Therapy by varying the pressure or composition of the atmosphere in which the patient lives.

aerotonometer An instrument to determine the pressure of gases in blood.